

Applicants: Romero et al.  
Appl. No.: 10/511,385  
Filed: October 15, 2004  
Supplemental Amendment  
Page 2 of 3

10/511 385 RP  
4/3/09

**IN THE SPECIFICATION:**

*Please insert the sequence listing after the specification but before the listing of claims.*

*Please insert the following paragraph on page <sup>34</sup>~~44~~, before the claims:*

RP  
4/3/09

**INCORPORATION OF SEQUENCE LISTING**

Incorporated herein by reference in its entirety is the Sequence Listing for the application.

The Sequence Listing is disclosed on a computer-readable ASCII text file titled,

“sequence\_listing.txt”, created on October 31, 2008. The sequence\_listing.txt file is 58kb in size.

10/5 11384

RP 4/3/09

proteins ~~with acknowledged~~ having known adjuvant activity ~~like~~, such as p64K<sub>1</sub> (R. Silva et al US 5286484 [[y]] and EP 0474313), or ~~can be~~ covalently bound to ~~them~~ adjuvants after their individual obtainment following the polypeptide synthesis. Other available ~~strategy~~ strategies in these cases ~~is~~ are the obtainment of the natural polypeptide, its mutated or modified variants, and their fragments, as a part of loops exposed or not in bacterial proteins like OMP1, which are part of immunostimulatory preparations, in this particular case VSSP (R.Perez et al US 5788985 [[y]] and 6149921). Furthermore it is possible to obtain the polypeptidic immunogen exposed in the surface of a viral particle (HbsAg, VP2 of parvovirus, etc.), bound to specific peptides that target cells or organs specialized in the induction of the immune response (CTLA4, Fc segment of the Ig, etc.), or to proteins capable of increasing biodistribution like VP22.

<sup>22</sup>  
On page 10 of the specification, please replace the paragraph beginning on line 7 with the following:

RP 4/3/09

Additionally, the gene of interest can be preceded by the coding sequence for the mRNA replication machinery, in a way that mRNA is amplified in the target cell, increasing the expression of said gene, and with it, ~~of~~ the therapeutic/vaccine effect according to the invention. The replication machinery in question could be of alphavirus origin (Schlesinger S, Expert Opin Biol Ther. 1:177, 2001), more specifically derived from the Sindbis or Semliki viruses, or similar. In this particular case, the gene of interest is under the transcriptional control of a subgenomic promoter that allows the amplification of its mRNA in target cells, once the molecules according to the present invention have been internalized. ~~Besides~~ Furthermore, the DNA vector might contain sequences that permit the replication of the molecules, which are object objects of the present invention, in mammalian cells. This allows an increase in the expression levels and/or of the therapeutic/vaccine effect (Collings A., Vaccine 18:4601, 1999).